# Physician, organisational and patient characteristics explaining the use of angiotensin converting enzyme inhibitors in heart failure treatment

Kasje, WN; Denig, P; Stewart, RE; de Graeff, PA; Haaijer-Ruskamp, FM

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PHARMACOEPIDEMIOLOGY AND PRESCRIPTION

Willeke N. Kasje · Petra Denig · Roy E. Stewart
Pieter A. de. Graeff · Flora M. Haaijer-Ruskamp

# Physician, organisational and patient characteristics explaining the use of angiotensin converting enzyme inhibitors in heart failure treatment: a multilevel study

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**Abstract** *Objective*: Heart failure treatment in general practice is not concordant with guideline recommendations. Insight into the key determinants at different levels is needed in order to improve care. The aim was to assess the influence of physician, organisational and patient characteristics on the treatment of chronic heart failure with angiotensin converting enzyme (ACE) inhibitors in primary care.
*Methods*: Physician and organisational data were collected by means of a questionnaire. Patient and treatment data were extracted from electronic medical records. Multilevel analysis was used to assess the effect of physician, organisational and patient factors on the treatment with ACE inhibitors in terms of prescription rate and dosage.
*Results*: Data from 735 randomly selected heart failure patients were extracted from the medical records of 95 general practitioners (GPs). Patients who visited a cardiologist or an outpatient heart failure clinic were more likely to receive an ACE inhibitor. In addition, relatively young patients, male patients and patients already using a diuretic were more likely to receive an ACE inhibitor. Furthermore, male patients and patients with concomitant hypertension were more likely to receive a higher dose of ACE inhibitor. GP characteristics did not determine whether CHF patients received ACE inhibitor treatment.
*Conclusion*: The differences in ACE inhibitor prescribing seem to be linked more to patient than physician characteristics. Interventions to improve the quality of care should therefore focus on the treatment of specific patient groups. Specialised care, particularly through outpatient clinics, could lead to improvement in the use of ACE inhibitors.

W. N. Kasje · P. Denig (✉) · P. A. Graeff
F. M. Haaijer-Ruskamp
Department of Clinical Pharmacology,
University of Groningen,
A. Deusinglaan 1,
9713AV Groningen,
The Netherlands
E-mail: p.denig@med.rug.nl
Tel.: +31-50-3633205
Fax: +31-50-3632812

W. N. Kasje · P. Denig · R. E. Stewart
F. M. Haaijer-Ruskamp
Northern Centre for Healthcare Research,
University of Groningen,
The Netherlands

R. E. Stewart
Department of Health Sciences,
University of Groningen,
The Netherlands

P. A. Graeff
Department of Internal Medicine,
Groningen University Hospital,
The Netherlands

## Introduction

Most guidelines on the management of chronic heart failure (CHF) recommend angiotensin converting enzyme (ACE) inhibitors as standard therapy for all patients [1]. Also, in patients whose diagnosis is based on signs and symptoms, as is usually the case in Dutch general practice, ACE inhibitors are considered standard long-term therapy after starting treatment with diuretics [2]. Although treatment pattern differs between countries [3], ACE inhibitors are generally underused and under-dosed in general practice [4–6].

Surveys have revealed a number of problems that general practitioners (GPs) perceive for optimal CHF management, such as difficulties with establishing an accurate diagnosis, lack of time and available resources, poor communication between primary and secondary care, and fear or reluctance to initiate ACE inhibitors in elderly and frail patients or patients already on diuretics [7–10]. Other studies focused particularly on specialist type or organisational factors, indicating that

cardiologists prescribe ACE inhibitors both more frequently and in a higher dosage than GPs do, and that patients attending heart failure clinics receive more adequate doses of ACE inhibitor than those in primary care [11–13]. Furthermore, several patient characteristics seem to be associated with heart failure management. Female and elderly patients were less likely to be referred to a specialist or to a hospital outpatient clinic, had less access to echocardiography and received less ACE inhibitor treatment [3, 14–16].

Most of these studies did not look at the combined influence of physician, organisational and patient factors, although it has been shown that there can be relevant differences in patient population at the physician or organisational level [12, 17]. Also within one level, characteristics such as the patient's age and gender are clearly related in the way they affect the management of heart failure [15]. Therefore, it is important to examine all variables simultaneously.

The aim of this study was to assess the influence of physician, organisational and patient characteristics on the quality of CHF treatment in primary care, focusing on the use and dosage of ACE inhibitors.

## Methods

### Study design and population

This study was part of the baseline of a larger study conducted from September 2001 to May 2002 in the north of the Netherlands, evaluating two audit programs for peer review groups focusing on the treatment of CHF and treatment of hypertension in diabetic patients [18].

The study was conducted in 21 peer-review groups with 150 GPs, of whom 95 GPs participated in this study. Physician and organisational characteristics were measured by a structured questionnaire. Patients with the following inclusion criteria were selected: all patients with a diagnostic code or the text 'heart failure', 'cardiac asthma', 'cardiac decompensation' or 'left ventricular dysfunction' in their medical records. From this list, a random sample of ten CHF patients per GP or practice was selected. All cases were screened to exclude both misclassification and those patients with diabetes mellitus as comorbidity. These patients were excluded because they fell into both the control and intervention group for the larger study. The GPs were asked to verify the CHF diagnosis.

Patient data were extracted by trained data extractors from GPs computerised medical records. Data were collected on prescriptions of cardiovascular medication, possible contra-indications for cardiovascular drugs and previous medication problems mentioned in the medical record. All prescriptions with a start date no more than 6 months prior to data collection were included. These data were recorded anonymously on a printed form which included the patient's sex and birth date. At the time of the study, no informed consent from patients was needed for this study.

### Outcome variables

The first outcome measure focused on whether an ACE inhibitor was prescribed or not. The second outcome measure was the average standardised dosage of the ACE inhibitors prescribed. ACE inhibitor dosages were converted to enalapril-equivalent dosages according to the target daily doses recommended for heart failure in the Dutch reference desk book. This method has been used previously [19] and uses enalapril 20 mg as reference dose with equivalent doses of captopril 150 mg, ramipril 10 mg, quinapril 20 mg, lisinopril 20 mg, fosinopril 40 mg and perindopril 4 mg.

### Determinants

Determinants included at the physician level were the GPs' gender, work experience ($<10$ years, 10–20 years, $>20$ years) and dispensing status (whether or not the GP is allowed to dispense drugs him/herself). Size and type of the practice (single-handed versus partnership) and location of the practice (urban, semi-urban or rural) were measured as organisational characteristics at the physician level. Organisational factors included at patient level were visits to a CHF outpatient clinic and hospitalisations in the previous year, and referrals to a cardiologist. Patient demographics included were age ($<85$ years or $\geq 85$ years) and gender. Other patient characteristics included were comorbidities documented in the medical record, such as cerebrovascular disease (stroke, transient ischaemic attack), hypertension, angina, peripheral vascular disease, atrial fibrillation, and the presence of chronic obstructive pulmonary disease (COPD) or asthma. In addition, serum creatinine above normal levels ($>80$ μmol/l for females and $>110$ μmol/l for males) and the use of a diuretic were included as factors, which may influence the choice of treatment. The use of diuretic was included since GPs have indicated that these drugs may form a barrier for prescribing an ACE inhibitor [20]. Finally, the objectivity of the diagnosis of heart failure was included in the model, since we included all patients who were diagnosed with CHF based on criteria defined by the GPs. An objective diagnosis was defined as having a registered ejection fraction below 40% and/or an echocardiography indicating heart failure or left ventricular dysfunction.

### Statistical analysis

Multilevel analysis was used to assess the influence of all characteristics simultaneously on each of the outcome variables. A two-level random intercept model was esti-

mated, taking into account the clustering of patients within the practice of a GP. Logistic regression was used for treatment with an ACE inhibitor as a dichotomous outcome variable. To estimate the effect of the determinants on average ACE inhibitor dosage, a regression model was built with the standardised dosage as a continuous outcome variable [21].

The intra-class correlation coefficient (ICC) was calculated to assess the variance at the physician level. When the ICC is nearly zero, a non-hierarchical regression model can be used. To evaluate whether the determinants in the model are a good fit for predicting the outcome variable, the deviance test was used comparing the final with the empty two-level model.

A possible interaction effect between age and gender of the patient was built into the treatment model, because it is known that older women in particular may receive more diuretics and fewer ACE inhibitors [14]. The influence of the cardiologist was analysed in two separate models—one including only referrals during the last year and one including all referrals during the last 3 years. This was done because a patient in The Netherlands may remain under the care of a cardiologist for longer periods without a new referral. Descriptive analyses were performed with SPSS 10 and multilevel analysis was analysed using MLwin1.2 [21].

## Results

### Characteristics of the population

Most of the 95 GPs were male (86%) and their mean age was 47 years (Table 1). The majority worked in a single-handed practice (59%) and in a rural area (63%). The theoretical number of 950 patients was not achieved, as not all practices could provide ten CHF patients due to the fact that some practices had a relatively young patient population. Furthermore, patients with a comorbidity of diabetes and misclassified patients were excluded. Of the remaining 735 CHF patients, 52% was male and their mean age was 76 years (Table 2). The average recorded duration of their heart failure was 3.3 years. An objective diagnosis (based on ejection fraction or echocardiography) was recorded for 78 patients (11%). In the previous year, 33% had been referred to a cardiologist; whereas 49% had a referral in the last 3 years. Only 3% visited an outpatient heart failure clinic.

Most CHF patients (67%) received a diuretic (Table 2); 47% were treated with ACE inhibitors and another 8% received an angiotensin-II antagonist. A noteworthy proportion of patients (10%) did not receive any CHF drug treatment. These patients had been referred to a cardiologist less often (18% in the previous year). The medical history of four patients not receiving an ACE inhibitor reported cough as the reason for stopping ACE inhibitor use. Other side effects were mentioned for another four patients as reasons to stop using an ACE inhibitor. For six patients, ACE inhibitors were discontinued without a documented reason in their medical record.

### Characteristics associated with ACE inhibitor therapy

The intra-class correlation coefficient (ICC = 0.061) in the multilevel model showed that there were differences

**Table 1** General practitioner and practice characteristics ($n$ = 95)

| | Mean ± SD | % |
|---|---|---|
| Age (years) | 46.9 ± 6.4 | |
| Male | | 86.3 |
| Work experience | | |
| < 10 years | | 29.0 |
| 10–20 years | | 32.3 |
| > 20 years | | 37.9 |
| Dispensing doctor | | 25.8 |
| Organisational characteristics | | |
| Single-handed practice | | 58.9 |
| Practice size | 2292.9 ± 526.6 | |
| Practice location | | |
| Urban | | 28.4 |
| Semi-urban | | 8.4 |
| Rural | | 63.2 |

**Table 2** Patient characteristics as registered in the medical records ($n$ = 735). *ACE* angiotensin converting enzyme, *COPD* chronic obstructive pulmonary disease, *CHF* chronic heart failure

| | Mean ± SD | $n$ | % |
|---|---|---|---|
| Age (years) | 76.3 ± 11.4 | 735 | |
| Creatinine (μmol/l) | 123.6 ± 67.7 | 248 | |
| Potassium (mmol/l) | 4.3 ± 0.6 | 207 | |
| Objective diagnosis [a] | | 78 | 10.6 |
| Duration of CHF (years) | 3.3 ± 3.2 | 446 | |
| Male | | 382 | 52.0 |
| Ejection fraction | 35.1 ± 14.1 | 43 | |
| Cerebrovascular disease | | 54 | 7.3 |
| Myocardial infarction | | 188 | 26 |
| Angina pectoris | | 207 | 28 |
| Atrial fibrillation | | 240 | 33 |
| Hypertension | | 235 | 32 |
| Peripheral vascular disease | | 32 | 4 |
| COPD or asthma | | 234 | 32 |
| Organisational characteristics | | | |
| Hospitalisation in previous year | | 143 | 20 |
| Specialist care in previous year | | 239 | 33 |
| Specialist care in previous three years | | 361 | 49 |
| Care by outpatient heart failure clinic in previous year | | 20 | 3 |
| Treatment (%) | | | |
| Diuretic | | 495 | 67 |
| ACE inhibitor | | 342 | 47 |
| AII-antagonist | | 58 | 8 |
| No medication | | 76 | 10 |

[a] Patients with a documented ejection fraction below 40% and/or an echocardiography confirming heart failure or left ventricular dysfunction

between GPs in prescribing frequency of ACE inhibitors. The deviance test for this treatment model was significant (Table 3, Chi-square = 50.13, df = 23, $P < 0.001$).

One organisational factor had a significant impact after adjusting for patient characteristics. Patients who visited a heart failure outpatient clinic had a higher chance of being prescribed an ACE inhibitor. In the model including all referrals to a cardiologist in the previous 3 years, patients who had been referred were also more likely to receive an ACE inhibitor. In the model including only referrals during the last year, this factor did not reach significance (model not shown). In this model, however, patients from dispensing GPs were found to be more likely to receive an ACE inhibitor (odds 1.64; 95% CI 1.04–2.61, model not shown). In both models, male patients, patients aged less than 85 years and patients who were using a diuretic had a higher probability of receiving an ACE inhibitor (Table 3).

Characteristics associated with ACE inhibitor dosage

Of the 320 patients who received an ACE inhibitor for which the dosage was registered, the average enalapril-equivalent dose was 13.5 mg. In the multilevel model predicting the ACE inhibitor dosage, the intra-class correlation coefficient was 0.018. The deviance test showed that the multilevel model including all factors did not provide a significant fit (Chi-square = 16.47, df = 23, $P > 0.05$). None of the determinants at the physician or practice level contributed to explaining the differences in dosages prescribed. Therefore, the results of a linear regression model at the patient level are presented (Table 3). After adjustment for other patient characteristics—including age—male patients were more likely to receive a high dosage than female patients. CHF patients with an additional comorbidity of hypertension were more likely to receive higher dosages of the ACE inhibitor.

**Table 3** Physician, organisational and patient factors predicting treatment with and dosage of angiotensin converting enzyme (ACE) inhibitors. *COPD* chronic obstructive pulmonary disease

| | Multilevel logistic model for treatment with ACE inhibitor ($n$ = 735) odds (CI 95%) | Linear regression model for dosage ACE inhibitor ($n$ = 320) regression coefficients (CI 95%) |
|---|---|---|
| Physician level | | |
| Physician characteristics | | |
| Gender (male) | 1.15 (0.64–2.07) | |
| Work experience < 10 years | 1.00 | |
| Work experience 10–20 years | 0.79 (0.48–1.29) | |
| Work experience > 20 years | 1.10 (0.68–1.76) | |
| Dispensing | 0.63 (0.39–1.01) | |
| Organisational characteristics | | |
| Practice type (single-handed) | 1.33 (0.85–2.09) | |
| Practice location urban | 1.00 | |
| Practice location semi-urban | 1.29 (0.62–2.67) | |
| Practice location rural | 1.32 (0.77–2.26) | |
| Practice size | 1.00 (0.99–1.00) | |
| Patient level | | |
| Patient characteristics | | |
| Age (≥85 years) | 0.55* (0.35–0.85) | 1.98 (−1.54–5.50) |
| Gender (male) | 1.60* (1.13–2.27) | 2.69* (0.20–5.19) |
| Objective diagnosis | 1.48 (0.98–2.81) | −1.70 (−5.52–2.12) |
| Myocardial infarction | 0.86 (0.57–1.28) | −1.70 (−4.50–1.10) |
| Hypertension | 1.29 (0.90–1.85) | 4.87* (2.35–7.40) |
| Peripheral vascular disease | 0.78 (0.33–1.84) | 2.10 (−4.34–8.55) |
| Atrial fibrillation | 1.20 (0.84–1.70) | −0.81 (−3.34–1.71) |
| Angina pectoris | 0.95 (0.65–1.40) | −1.98 (−4.67–0.70) |
| COPD or asthma | 0.87 (0.61–1.26) | −0.99 (−3.63–1.65) |
| Cerebrovascular diseases | 0.77 (0.41–1.45) | −3.22 (−8.03–1.60) |
| Creatinine > normal | 1.19 (0.79–1.78) | −1.22 (−3.97–1.52) |
| Diuretic | 1.89* (1.32–2.71) | −2.27 (−5.03–0.50) |
| Interaction term gender-age | 0.50 (0.21–1.18) | |
| Organisational characteristics | | |
| Hospitalisation | 1.40 (0.90–2.19) | −1.27 (−4.26–1.72) |
| Outpatient heart failure clinic | 4.58* (1.45–14.47) | 2.78 (−3.25–8.81) |
| Referral to cardiologist (< 3 years) | 1.85* (1.28–2.68) | −1.37 (−3.83–1.09) |

*Significant at $P < 0.05$ level

## Discussion

### Summary of main findings

Underuse and under-dosing of ACE inhibitors were mainly associated with patient characteristics, such as gender, age, concomitant hypertension and the use of a diuretic. Organisational factors as specialist care and outpatient heart failure clinics were also associated with higher prescribing of ACE inhibitors. General GP characteristics, such as work experience or gender, did not determine whether heart failure patients received ACE inhibitor treatment.

### Strengths and limitations

Quality of care may be influenced by factors that are related to the patients, the physicians or the way that the care is organised. In this study, these characteristics were studied in one model thereby taking into account possible confounding factors at different levels.

Our study does have some limitations. The population of GPs in our study, including a relative large proportion of single-handed, male, dispensing GPs, is typical for our region. This regional selection may influence drawing conclusions about the quality of treatment in general, but it does not limit the analysis of factors influencing this quality. Excluding the subgroup of CHF patients with concomitant diabetes from our study forms a limitation since ACE inhibitors are prescribed more frequently in this group of patients [5]. The use of medical records implies that only clinical information known and considered relevant by the GPs has been included; therefore under-recording of normal findings in particular was likely [12]. In our analyses, we assumed that no registered measurement implied no abnormal finding, but some of these patients may have had an undocumented abnormal finding. Prescriptions were made electronically by the GPs in our study and were automatically recorded in the medical records. Initial prescriptions of specialists may have been missed; in the Netherlands, it is common for chronic medication started by a specialist to be continued by the GP and recorded in the medical records. In the case of dispensing GPs, initial prescriptions of specialists are more often included in the GPs' medical records. Data on ejection fraction, i.e. on an objective diagnosis of CHF, were available for only a few patients. This reflects reality in primary care in The Netherlands, where GPs tend to diagnose heart failure on clinical grounds, supported by a diagnostic trial of diuretics [22]. In the European IMPROVEMENT-HF study in primary care, only 10% of Dutch primary care physicians would ask for an echocardiography [3]. This may be a consequence of the older Dutch general practice guideline (1995) that still stated, at that time, that echocardiography is of limited value for the diagnosis of heart failure. However, the newer guideline (2002) does indicate the need for echocardiography, as well as open access of GPs to echocardiography. In addition, when diagnostics have been performed (as is the case in referred patients), it seems that GPs do not record such data adequately in the (computerised) medical records [3]. In this study, we sought to examine the current prescription for those patients the GP considered as having CHF. We focused on the prescription of ACE inhibitors only. The results of this study can therefore not be extrapolated to the overall treatment of CHF. The use of ACE inhibitors, however, is one of the relevant performance indicators for CHF [23, 24].

### Comparison with existing literature

A beneficial effect on the use of ACE inhibitors could be demonstrated when patients had attended an outpatient heart failure clinic, although this involved only a small percentage of patients. It has been suggested that, given the complicated treatment of heart failure and comorbid diseases, heart failure clinics with their multifaceted approach may be better equipped for treating CHF patients than GPs alone [25]. Our findings also show that previously described differences observed in treatment patterns between GPs and cardiologists remain significant after adjustment for differences in patient population. Patients with a referral to a cardiologist in the last 3 years were more likely to receive an ACE inhibitor. The finding that patients of dispensing GPs received more ACE inhibitors when only including referrals in the previous year may be an artefact related to the fact that initial prescriptions of specialists are more often included in the medical record of these dispensing GPs.

The diagnosis of heart failure in general practice is often based on symptoms and signs [22]. Echocardiography is not as readily available in The Netherlands as in other countries such as the UK [26]. In our study, the recording of an objectively made diagnosis based on an echocardiography or ejection fraction was associated with a somewhat higher use of ACE inhibitors, but this was not significant. It should be noted, however, that we adjusted for specialist care, and there were only nine patients who had an objective diagnosis without such specialist care.

The finding that elderly patients were prescribed fewer ACE inhibitors than younger patients has been shown several times before. The GPs seem reluctant to prescribe these drugs in heart failure patients aged 85 years and over, despite recent findings showing their benefits in very old and frail patients [27]. After adjusting for age, female patients were also less likely to receive ACE inhibitors. This is in contrast to a previous study where the influence of gender decreased after controlling for age [16], but in line with a large international study [3]. Our findings did not support the concept that women are less likely to receive ACE

inhibitor treatment because of a lower referral rate [28]. It therefore seems more likely that low ACE inhibitor use in these patients is explained by a general attitude of using less aggressive treatment in female patients. This notion is strengthened in our study by the finding that, even after adjusting for age, female patients were also more likely to receive a lower ACE inhibitor dose.

Patients receiving diuretics had a greater chance of receiving an ACE inhibitor after adjustment for other comorbidities. Most treatment guidelines recommend prescription of an ACE inhibitor in addition to a diuretic, but GPs have expressed the fear of hypotension and some reluctance to start an ACE inhibitor in patients already using diuretics [9, 20]. Apparently, these concerns do not prevent them from prescribing ACE inhibitors. Patients with a comorbidity of hypertension were more likely to receive a higher ACE inhibitor dose. This relationship between concomitant hypertension and target dose has been observed previously [29] and may indicate that GPs are less concerned about high dosages when the patients also have hypertension.

We found few indications that the underuse of ACE inhibitors could be attributed to previous problems with these drugs in individual patients. Only for 14 patients could we determine that an ACE inhibitor had been discontinued with or without a documented reason. The use of angiotensin-II-antagonists, which may be considered as an alternative for patients who cannot tolerate ACE inhibitors, was small. Of the CHF patients in our study, 10% were not using any heart failure medication. It has been suggested that such under-prescribing occurs especially in patients with relatively minor complaints, i.e. NYHA classes 1 and 2 [30].

## Implications for clinical practice

Patient characteristics such as being a female, older age and no referral to secondary care were related to under-prescribing and under-dosing with ACE inhibitors, while physician characteristics such as physician gender or experience were not relevant. Interventions in general practice should therefore not be aimed at specific GPs, but at specific patient groups and should aim to improve the quality of care especially for women, elderly and patients without comorbidity. Specialised care, for instance through outpatient clinics, could lead to improvement of heart failure treatment.

Outside the main focus of this study, these results indicate the need for better diagnostics in general practice and better recording of these data to achieve a more objective diagnosis of CHF.

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